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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS	4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS	5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS	6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS	7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS	8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS	9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS	10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS	11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS	12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS	13	OCT 19	E-mail format enhanced
NEWS	14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS	15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS	20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available

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=> e hoekstra, m/au
E1            2     HOEKSTRA YDO N/AU
E2            3     HOEKSTRA YKE/AU
E3            0 --> HOEKSTRA, M/AU
E4            1     HOEKSTRAEN A/AU
E5            2     HOEKSTRAL J B L/AU
E6            3     HOEKSTRAOUSSOREN S J F/AU
E7            2     HOEKSTRASCHUMAN M/AU
E8            1     HOEKSTRASS K E/AU
E9            1     HOEKSTRAVANDALEN R A H/AU
E10           1     HOEKSTRAWEEBERS J E H M/AU
E11           1     HOEKTRA E J/AU
E12           1     HOEKVELD G A/AU

=> s HECT E3 ubiquitin ligase
MISSING OPERATOR

=> s (HECT E3 ubiquitin ligase WW domain)
MISSING OPERATOR

=> s (ubiquitin ligase)
L1       12510 (UBIQUITIN LIGASE)

=> s l1 and (WW domain)
L2         212 L1 AND (WW DOMAIN)

=> s l2 and (HECT)
L3         104 L2 AND (HECT)

=> s l3 and (E3)
L4           0 L3 AND ("HOEKSTRA, M"/AU)

=> s l3 and (Smad protein)
L5          34 L3 AND (SMAD PROTEIN)

=> s l5 and (PY motif)
L6          34 L5 AND (PY MOTIF)
```

=> s l6 ti abs ibib 1-15
MISSING OPERATOR L6 TI
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d l6 ti abs ibib 1-15

L6 ANSWER 1 OF 34 USPATFULL on STN
TI Methods for modulating signal transduction mediated by TGF-beta related proteins
AB Methods are provided for identifying agents that modulate signaling mediated by transforming growth factor beta (TGF-β) and members of the TGF-β family, such as bone morphogenic protein (BMP). Such agents may be identified using screens that evaluate candidate agents for the ability to modulate Smad protein degradation. Agents identified as described herein may be used to augment or inhibit signaling mediated by one or more TGF-β family members in a variety of cell types and for therapeutic purposes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:173228 USPATFULL
TITLE:	Methods for modulating signal transduction mediated by TGF-beta related proteins
INVENTOR(S):	Hoekstra, Merl F., Cardiff-by-the-sea, CA, UNITED STATES Xie, Weilin, San Diego, CA, UNITED STATES Murray, Brion W., San Diego, CA, UNITED STATES Mercurio, Frank M., Del Mar, CA, UNITED STATES
PATENT ASSIGNEE(S):	Signal Pharmaceuticals, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003119072	A1	20030626
APPLICATION INFO.:	US 2002-307956	A1	20021202 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-385918, filed on 30 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711		
NUMBER OF CLAIMS:	54		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	12 Drawing Page(s)		
LINE COUNT:	1625		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83047 peptide DGENE
AB The present sequence is the HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase HECT domain.
The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3

ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83047 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human WWP1 HECT E3 ubiquitin ligase HECT domain.

L6 ANSWER 3 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83046 peptide DGENE
AB The present sequence is the HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase HECT domain.
The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83046 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]

DESCRIPTION: Human WWP1 HECT E3 ubiquitin ligase HECT domain.

L6 ANSWER 4 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83045 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.
ACCESSION NUMBER: AAB83045 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif mutant Nedd peptide.

L6 ANSWER 5 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83044 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by

E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83044 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif Nedd peptide.

L6 ANSWER 6 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83043 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83043 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829

PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif WBP1 peptide.

L6 ANSWER 7 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83042 peptide DGENE
AB The present sequence is a muated Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.
ACCESSION NUMBER: AAB83042 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Mutated human Smad 1 PY peptide.

L6 ANSWER 8 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83041 peptide DGENE
AB The present sequence is the WW domain of the HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase WWP1. The WW domain binds to the Smad PY motif, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of

an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83041 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human HECT E3 ubiquitin ligase WWP1 WW domain.

L6 ANSWER 9 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83040 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83040 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -

INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #6.

L6 ANSWER 10 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83039 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.
ACCESSION NUMBER: AAB83039 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #5.

L6 ANSWER 11 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83038 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3

ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83038 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #4.

L6 ANSWER 12 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83037 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.
ACCESSION NUMBER: AAB83037 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic

protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #3.

L6 ANSWER 13 OF 34 DGENE COPYRIGHT 2006 The Thomson Corp on STN
TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83036 peptide DGENE
AB The present sequence is a Smad PY motif. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.
ACCESSION NUMBER: AAB83036 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #2.

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TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83035 peptide DGENE
AB The present sequence is a Smad PY motif. The

PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer, inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83035 peptide DGENE
TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M
PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.
PATENT INFO: WO 2001016604 A1 20010308 75
APPLICATION INFO: WO 2000-US23729 20000829
PRIORITY INFO: US 1999-385918 19990830
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-327913 [34]
DESCRIPTION: Human Smad PY motif #1.

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TI Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -
AN AAB83034 peptide DGENE
AB The present sequence is a Smad PY motif consensus sequence. The PY motif binds to the WW domain of HECT (homologous to E6 carboxyl terminus) E3 ubiquitin ligase, resulting in ubiquitination of Smad by the E3 ubiquitin ligase. The sequence is provided in a specification relating to a method for screening for agents that modulate transforming growth factor (TGF)-beta and/or bone morphogenic protein (BMP)-mediated signalling. The method involves evaluating the effect of an agent on binding of HECT E3 ubiquitin ligase WW domain to Smad PY motif, on ubiquitination of Smad protein by E3 ubiquitin ligase, or on the cellular levels of Smad protein HECT E3 ubiquitin ligase activity. The method is useful for stimulating bone formation in a patient or treating a condition associated with insufficient TGF-beta and/or BMP-mediated cell signalling. Agents that inhibit BMP-mediated signalling are useful for treating inflammation, ageing, cancer and infectious diseases. Agents that augment BMP-mediated signalling are useful for stimulating bone anabolism as well as treating broken bones, osteoporosis, and acute or chronic renal failure. Agents that inhibit TGF-mediated signalling are useful for treating cancer,

inflammation, neurodegeneration and fibrosis.

ACCESSION NUMBER: AAB83034 peptide DGENE

TITLE: Screening for modulators of TGF-beta and/or bone morphogenic protein (BMP) mediated signaling useful for treating cancer and osteoporosis by evaluating the ability of agents to modulate Smad protein degradation -

INVENTOR: Hoekstra M F; Xie W; Murray B W; Mercurio F M

PATENT ASSIGNEE: (SIGN-N)SIGNAL PHARM INC.

PATENT INFO: WO 2001016604 A1 20010308 75

APPLICATION INFO: WO 2000-US23729 20000829

PRIORITY INFO: US 1999-385918 19990830

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2001-327913 [34]

DESCRIPTION: Human Smad 2 and Smad 3 PY motif consensus sequence.